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# Motor cortex stimulation for enhancement of recovery after stroke: Case report

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*We present a case report of a 65-year-old patient who had a subcortical infarct and a right spastic hemiparesis that occurred 19 months before being treated with an investigational therapy consisting of low frequency subthreshold epidural motor cortex electrical stimulation delivered during structured occupational therapy repeated daily for three weeks. Before treatment the patient's affected arm rested in a flexion posture and he was unable to flex or extend the fingers. After three weeks of treatment, the resting tone of his arm had improved and he was able to grasp a pen and write letters. The Fugl-Meyer motor scale score improved from 36 to 46 and this improvement was sustained for four weeks after the conclusion of rehabilitation therapy. This is the first patient to be entered into a randomized clinical feasibility and safety study assessing functional improvement in stroke patients treated with epidural cortical stimulation concurrent with occupational therapy (an investigational therapy). [Neurol Res 2003; 25: 815–818]*

*Keywords: Stroke; electrical stimulation; motor cortex; rehabilitation*

## INTRODUCTION

Pre-clinical evaluation, in both rodent and primate stroke models, of the functional improvement provided by subthreshold epidural cortical stimulation (CS) of cortex adjacent to damaged motor cortex shows significant functional improvements. (see companion papers in this issue). These investigations were performed because of a number of anecdotal reports noting improved motor function in patients being treated for central pain that had developed after thalamic infarction<sup>1–3</sup>. The Wayne State University Institutional Review Board approved this clinical trial sponsored by Northstar Neuroscience, Inc. (Seattle, WA, USA) to evaluate the safety of CS concurrent with occupational therapy in patients with a chronic neurological deficit from either cortical or subcortical stroke. The Food and Drug Administration has approved an Investigational Device Exemption (IDE) for this feasibility study. This case report presents results from the first subject entered into this randomized clinical trial.

## CASE REPORT

A 65-year-old, right-handed male developed a subcortical cerebral infarction. A right hemiparesis was present with his right arm more severely affected than his leg. He had co-existing adult onset Diabetes Mellitus and hypercholesterolemia. Initially he was treated with physical and occupational therapy that improved his

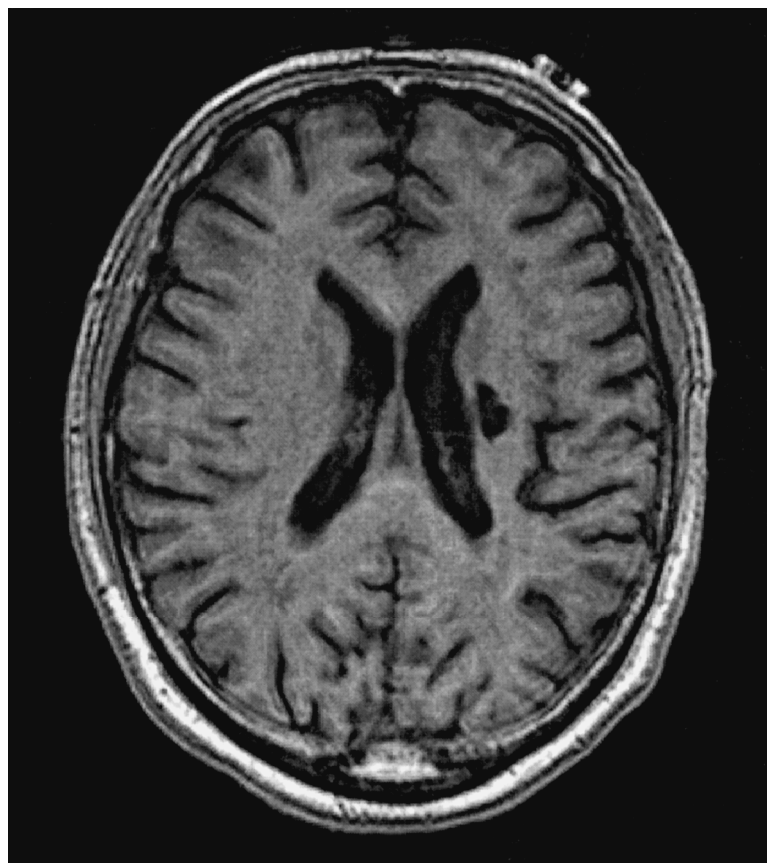
arm and leg function, but the improvement stabilized. Despite therapy, he was only able to extend his wrist against gravity. There was no voluntary finger flexion or extension.

Nineteen months after his stroke he was enrolled in the clinical study after meeting extensive entrance criteria. Some relevant baseline data were: arm Fugl-Meyer score 36/66, the (normalized) Stroke Impact Scale Handicap was 35/100. An anatomic magnetic resonance imaging study (MRI) showed a sub-cortical infarct lateral to the mid-body of the lateral ventricle (*Figure 1*) and his functional MRI (fMRI) performed while extending the right wrist at preset intervals localized the site of activity in the pre-central gyrus of the affected hemisphere (*Figure 2*).

After randomization to surgical treatment, a craniotomy flap was created using neuronavigational technique and sited over the region corresponding to the center of pre-central BOLD activity seen on fMRI identifying the motor cortical representation of wrist flexion. An investigational epidural 3×3 plate grid electrode array (Northstar Neuroscience Inc., Seattle, WA, USA) was implanted. Stimulation through selective electrode contacts evoked contralateral finger flexion confirming placement on the primary motor cortex. This also confirmed that direct cortical spinal projections were intact although the patient could not voluntarily control finger movement. The electrode lead was tunneled to a sub clavicular exit site and the craniotomy flap replaced.

Three days after surgery the patient began an intensive routine of daily occupational therapy directed at improving activities of daily living and involving the

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**Figure 1:** T1 weighted MRI demonstrating infarct just lateral to the mid-body of the lateral ventricle. This scan was taken 19 months after the patient's stroke

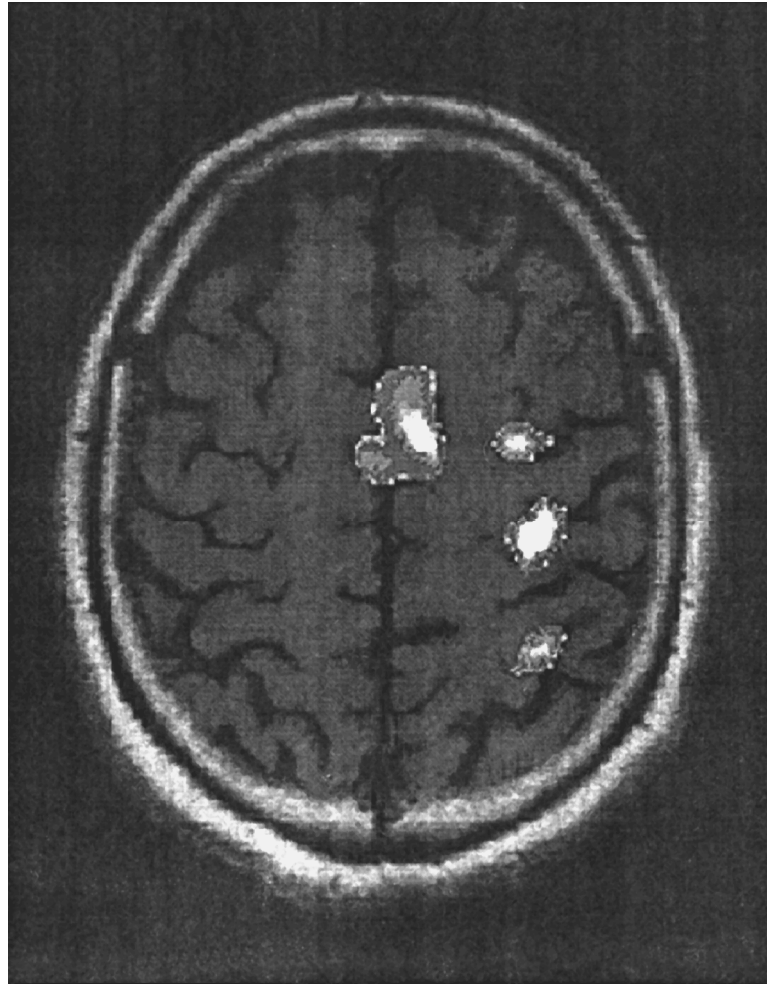
paretic hand and arm. During these sessions an investigational external pulse generator was attached to the electrode lead and worn in a chest harness, and sub-threshold cortical stimulation was delivered concurrent with occupational therapy. At the end of each daily session, the pulse generator was turned off and removed. During stimulation the pulse generator was set to deliver continuous stimulation at a rate of 50 Hz, pulse duration of 100 sec, and a current level of 4.5 mA.

During the three weeks of therapy, the patient showed improvement in pincer movement of the thumb and first finger, which he had not been able to do prior to electrode implantation and stimulation. By the end of the three weeks, his arm Fugl-Meyer motor scale score had improved from the baseline value of 36 points (of a total possible score of 66) to 46 at the one-week post-therapy follow-up visit. His normalized Stroke Impact Scale (SIS; for handicap) improved from a baseline level of 35 (maximum possible score of 100), to a post-treatment level of 75. The normalized SIS strength scale improved from a baseline of 42 to 75 four weeks after cessation of treatment. The occupational therapist and the attending neurologist observed other changes that could not be objectively documented in outcome measures. For example, the patient's upper extremity flexor posture gave way to a more natural posture,

although the Ashworth Spasticity Scale did not demonstrate any significant change. The 9-Hole Pegboard Test was also an outcome measure. There was no significant change in the pre- to post-therapy scores, because the patient's disability was too great to participate in this task. At the end of therapy he could pick up a pencil and print block letters and he could pick up a ball bearing. Both tasks were impossible before therapy one month earlier. This study was primarily performed to evaluate the safety of cortical stimulation to enhance motor recovery after stroke. There were no adverse effects related either to the surgery or to the cortical stimulation.

## DISCUSSION

This is a report of the first patient to be treated by an investigational restorative neurosurgical procedure designed to enhance recovery of the functional injury that occurs after stroke. The study extends observations made of motor improvements during treatment of central pain and information gained from pre-clinical studies (see companion papers in this issue) showing that subthreshold electrical stimulation of perilesion cortex concurrent with behavioral training can lead to the return of a significant portion of lost function. This appears to be due to neuroplasticity but the underlying



**Figure 2:** fMRI images demonstrating four areas of activation as a result of a wrist extension paradigm during scanning. The largest area corresponds to the SMA, a small activation area exists just anterior to the pre-central gyrus, a larger area in the posterior portion of the pre-central gyrus, and a smaller area in the parietal region

basis for this neuroplasticity is not completely understood. The pre-clinical data suggests that it may involve increasing or facilitating the effectiveness of cortical projections to the appropriate spinal segments.

These data from our first human subject indirectly support this neuroplasticity hypothesis. Although the patient had no willful finger function prior to therapy, the area targeted for stimulation corresponded to the pre-central gyrus involved with the only hand function the patient was capable of performing – wrist extension. This was first demonstrated by fMRI. What was intriguing about this stimulation was that a brief train of pulses delivered intra-operatively evoked individual finger flexion, thus implying that the cortico–spinal projection remained intact. The synaptic connections needed to willfully execute movements via this final common pathway were either not intact before stimulation, or were incapable of initiating movement. It is hypothesized that the sub-threshold electrical stimulation at the time of occupational therapy may depolarize the underlying neurons to a level that previously

ineffective pathways became capable of eliciting movement. As the synaptic circuits are reinforced by structured rehabilitation, their efficiency improves, leading to the improved ability to flex and extend otherwise paretic muscles.

Animal data also suggests that CS induces new dendrite formation<sup>4</sup>. New dendrites may form functional synapses leading to motor improvements. Primate and rodent studies<sup>5</sup> have shown that CS induces changes in the motor cortical representation areas so that uninjured areas of the motor cortex take on increased function of the damaged motor cortex. The anatomical and motor cortex representation area changes observed in animals may also occur in humans leading to enhanced recovery of function.

It is interesting that this first patient had a subcortical stroke. From a large series of patients treated with motor cortex stimulation for refractory pain, Katayama *et al.*<sup>6</sup> reviewed the results of treatment of 50 patients with a variety of concomitant movement disorders. For many of these patients subcortical stroke was the presumed

etiology of both their pain and movement disorders. A few of these patients also suffered hemiparesis as a result of the lesions. Anecdotally, Katayama noted that several of these patients' paresis improved following CS for pain control. The clinical outcome of these patients was probably similar to our first patient in the study.

## CONCLUSION

Although preliminary, the results presented here suggest that there is the potential to enhance motor recovery after stroke that occurred months to years earlier.

## ACKNOWLEDGEMENTS

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